ACVP Exam

- 2 Part Certification Exam
- 2017 First year Phase II exam in Tampa, FL
- Critical Tasks for Entry-Level Anatomic Pathologists
- Be familiar with Critical Tasks: When to use ancillary tests; Which and how to interpret those tests; ie flow cytometry, IHC, cytology
- 40% of Phase II: 20% of Phase II image-based MCQs
- Give appropriate disease, differential dx, list causes; pathogenesis; give clinpath or macro changes in other organs.
Laboratory Animal Diseases Encompass Many Animal Species......

This specialty embraces mammalian and non-mammalian species. Non-Human Primates, Dogs, Cats, Fish, Birds, Ruminants, Ferrets, Rabbits, Rodents (all types, **NOT** just rats and mice), Amphibians, Swine,

Yet, > 90% of all animals used in research are mice and rats

**Laboratory Animal Diseases**

Loose graphical interpretation of clinical disease

- **Spontaneous Disease / Trauma**
- **Experimental Disease**
- **Domestic Animal Disease**
- **Wild Animal Disease**

Why so few domestic/wild animal diseases?
Help with Mouse ID by Coat Color

Common White Mice
- Swiss mice (outbred)
- BALB/c
- FVB
- A and AKR mice

Common Black Mice
- C57BL/6

Common Brown Mice
- DBA-1 and DBA-2 mice
- C3H
- 129

Available for download or as a poster from the Jackson Laboratories.

Starting with the MOUSE........

First Question Asked: **Was the animal manipulated?**

Second Question Asked: **What is the background strain?**

**What is that 2nd question asking?**

BALB/c  C57BL/6 What background strain?

One Mouse is NOT just Like Another! Pay attention to genetic background

Regardless of the method of generation of mutations(s) and mutants, phenotypes are impacted by:
1. Genetic influences of the background strains
2. Infectious agents, microbiota and other environmental factors
Phenotypes to Expect | When to Expect
--- | ---
Malocclusion | Young Mice (by weaning)
Hydrocephalus | Especially in C57BL
Microphthalmia | Expect in C57BL; right eye in females
Sexual dimorphisms | Various Ages
Blind/Deaf | Various Ages
Dermatitis: Imperforate Vagina | Various Ages
Hydronephrosis | Various Ages
Vestibular Syndromes | Various Ages
Acidophilic Macrophage Pneumonia | Older Mice
Amyloidosis | Older Mice
Glomerulonephritis | Older Mice
Polyarteritis | Older Mice
Tumors | Older Mice

**SYNOPSIS**

### Eye & Skin

**Skin:** Ulcerative Dermatitis

*Mouse Ulcerative Dermatitis (MUD)*

Interferes with a lot of research

Secondary phenotypes:
- Leukocytosis
- Lymphadenopathy
- Splenomegaly
- Amyloidosis
- Glomerular Nephritis
- Sick mice
- Mortality
- C57BL > others

**Predisposing factor:**

- Genetic: (C57BL/6)
- or could be *ectoparasite sensitivity*
- secondary bacterial infection (Staph aureus or S. epidermidis)

*Adams et al., "A 'Pedi cures all: Toenail trimming and the treatment of ulcerative dermatitis in mice. Plos One, 1/2016*

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**Questions???

1. What is the bacterial agent that affects immunocompromised rodent animal models?
   - a. *C. kutcheri* that will spread through the colony
   - b. *S. pneumoniae*. Respiratory infection outbreak
   - c. Pseudoloma. Affect data interpretation
   - d. *C. bovis*. Will the animal model retain its same level of immunodeficiency?

2. Eosinophilic crystalline pneumonia is especially prevalent in which 2 strains of mice?
   - a. BALB/c and C57BL/6
   - b. 129/SvJ and C57BL/6
   - c. DBA1 and DBA2
   - d. FVB and BALB/c

3. Murine norovirus causes what clinical signs in immunocompetent mice?
   - a. Weight loss
   - b. None
   - c. Ruffled fur
   - d. Hunched posture

4. What is the name of the mouse paramyxovirus?
   - a. Sendai Virus
   - b. PVM
   - c. Ross River Virus
   - d. K virus

5. A common (and problematic) parasitic infection is?
   - a. Spironucleus muris
   - b. Rodentolepis nana
   - c. Chilomastix bettencorti
   - d. Syphacia obvelata
Skin: Ringtail

Primary lesion is a cornification disorder, retention hyperkeratosis and abnormal desquamation

Previous etiology: low humidity
Low incidence: 0.075%

Name the Condition: Barbering

Considered as a model of Trichotillomania. Dominant. Vibrasse
Many mice derived from the outbred Swiss mice have retinal degeneration. FVB mice, though born normal, have progressive retinal degeneration, and by weaning can be blind. Affected strains are: C3H, SJL, SWR, FVB.

Morphological Dx?

Unilateral Hardarian Gland Adenoma with exophthalmus

Morphological DX?
**Morphological DX?**

**Focal Aural Squamous Papilloma**

*Cause: Carcinogen; Murine papillomavirus*  
*Ingle, 48:500-505, 2011 Vet Pathol*

**Morphological DX?**

**Unilateral pinnal Fibrosarcoma**

**Morphological DX?**

**Icterus**  
Ear, skin and of the eye – as would be stated in other animals

**Name the Condition?**

*Note Barbering...*
Barbering
↓
Mastication/Fragmentation of Hair
↓
Fragments Penetrate and Expand the Gingival Sulcus
↓
Staphylococcal Organisms Carried into the Submucosa
↓
Abscess Develops
↓
Bone Dissolution

**Condition:** Botryomycosis or Facial Abscesses.
**Cause:** S. aureus or Pseudomonas aeruginosa;
Will see pyogranulomatous perinasal dermatitis, folliculitis - furunculitis

**Name the condition?**
**Etiology:**
**Predisposing factor?**
**Differential?**

**Name the condition?**
**Etiology:**
**Predisposing factor?**
**Differential?**

**Name the condition?**
**Etiology:** C. bovis
**Predisposing factor?**
Immunodeficiency (NOT hairlessness)
**Differential?** *Staphylo*us
Russo et al, Diffuse scaling dermatitis in an athymic nude mouse, Vet Pathol 722-6, 2013

**Morphologic Dx? Cause? Differential Dx?**
**Morphologic Dx?**
Focal, Dorsal, Cervical, Ulcerative Dermatitis with Cicatrization

**Cause?** Fur mites (Myobius musculi; Myocoptes musculinus; Radfordia affinis)

**Differential Dx?** Trauma; bacterial infection: S. aureus; S. xylosus, group G Strep spp.

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**Morphologic Dx?** Cutaneous Fibroma with multifocal ulceration

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**Morphologic Dx?** Cutaneous Fibroma with multifocal ulceration

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**Morphological Dx?** Demal Coccygeal Neural Crest Tumor

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**Morphological Dx?** Demal Coccygeal Neural Crest Tumor
Morphological Dx? **Dermal Coccygeal Neural Crest Tumor**

Mouse Strain?
- FVB mice
- Other

Common Location?
- Pinna of ear

Multiple pigmented tail masses

Diagnosis?

Hair follicle tumor; Association with GLI-1 overexpression? Polyomavirus? (seldom seen in barrier colonies)?
Morphologic Diagnosis? Preputial gland; unilateral to bilateral preputial gland abscess or suppurative preputial adenitis

Cause? Pasteurella pneumotropica; Klebsiella oxytoca; Staph spp.; Strep spp.

Morphologic Diagnosis? Diffuse, subcutaneous edema (anasarca)

Cause? Glomerular or intestinal amyloidosis; atrial thrombosis
Morphologic Diagnosis?
Focal, subcutaneous angio-lymphangiosarcoma
Second morphologic Diagnosis? Unilateral preputial gland abscess

What is this?

Nude mouse with bilateral tumor xenografts (patient-derived, or cell line), with unilateral ulceration.

Mammary Gland
Morphologic Diagnosis?
Predisposing or associated factors?

Pregnancy,
Pituitary pars distalis prolactinoma (FVB)
Radaelli, Vet Pathol, 2009

Spontaneous Mouse Mammary Tumors
C3H mouse strain has greatest propensity

Morphologic Diagnosis? Mammary Gland Hyperplasia
Predisposing or associated factors? Pregnancy,
Pituitary pars distalis prolactinoma (FVB)
Radaelli, Vet Pathol, 2009

What other tissues/conditions must be considered?
Morphologic Dx? Mammary gland adenocarcinoma

Cause? Mouse mammary tumor retrovirus (MMTV); carcinogens; hormones; strain-associated (C3H)

What other tissues/conditions must be considered? Salivary glands and cervical lymph nodes

Differential Diagnoses?
1. Salivary gland myoepithelioma
2. Mammary gland adenocarcinoma
3. Lymphoma

What might help you at necropsy with the correct diagnosis?

Thorax: Cardiovascular & Lung
Morphologic Diagnosis?
What strain of mouse do you think this is?

NOD mouse
Typically thymic lymphoma. If a known NOD mouse, will also see that the immune function is compromised; if a NOD-SCID – no T and B cells; poor APC function, decreased innate immunity. If strain is unknown, however could be a thymoma... (requiring microscopic examination)

Morphologic Dx?
Affected strains?
Histochemical stain to support your Dx?

Morphological Dx?
Locally extensive epicardial mineralization
Affected strains?
BALB/c (especially Byj substrain, Comparative Med 63:29-37, 2013); C3H, DBA
Histochemical stain to support your Dx? Von Kossa; Alizarin Red
Morphologic Diagnosis? Left: Auricular thrombosis with eccentric hypertrophy (noted below, right).

Possible etiologies?
Top: Pneumocystis murino; acidophilic macrophage pneumonia; Pneumonia (paramyxovirus) virus of mice; Sendai (paramyxovirus) virus in immunodeficient mice; Mouse norovirus in immunodeficient mice.
Bottom: Multifocal pulmonary abscesses or pyogranulomas; embolic Streptococcus or Staphylococcus.
Likely Morphological Dx?

Focal pulmonary adenoma and lobar acidophilic macrophage pneumonia (left lobe)

**Signalment**

Adult female C57BL/6 mouse

**Hyalinosis in other tissues:** nose, stomach, gall bladder; crystals in marrow, spleen - macrophages, PMNs

**Thoolen, B., R. R. Maronpot, et al. (2010).**

**Proliferative and Nonproliferative Lesions of the Rodent Hepatobiliary System.** Tox Path. 2010;38:5S

**Eosinophilic Crystalline Pneumonia as a Major Cause of Death in 129S4/SvJae Mice**

M. J. HOENERHOFF, M. F. STAROST, AND J. M. WARD Laboratory of Cell Regulation and Carcinogenesis, National Cancer Institute (M.JH); Division of Veterinary Resources, Office of Research Services (MFS); and Comparative Medicine Branch, National Institute for Allergy and Infectious Diseases (JMW), National Institutes of Health, Bethesda, MD


**Abdomen & Systemic Conditions**
Morphological Dx? Associated Findings?

Multiple Lymphomas

Preceding: (LN, thymus, spleen; above left – thymus; above: liver, spleen, Peyer’s patches & LN; A1 left: Peyer’s patches; near left: Thymic lymphoma in a SCID mouse

Associated findings: Renal tubular hyaline droplets (Fox Path 40:651-655, 2012); Possibly hypercalcemia of malignancy and osteolysis

Morphological Dx? Associated Findings?

Histiocytic Sarcoma

May be associated with renal tubular hyaline droplets (lysozyme overload);
hepatic extramedullary hematopoiesis (erythroid);
dysmyelopoiesis (decreased myeloid / increased erythroid)
Morphological Diagnosis?
Possible Cause?

Morphological Diagnosis: Multifocal to coalescing suppurative to necrotizing hepatitis
Possible Cause: Clostridium piliforme; Polytopic mouse hepatitis virus (Coronavirus); Ectromelia (Mouse Orthopox) virus; Salmonellosis, Reovirus-3 (infants); cytomegalovirus (infants); Adenovirus (infants)

Morphological Dx? Causes?

Hepatocellular adenoma
Causes:
Genetics (most commonly aged males, especially A and DBA mouse strains; Helicobacter hepaticus infection has been associated with an earlier onset and higher prevalence among A strain mice; Carcinogens
**Morphological Dx?**

**Hepatocellular adenocarcinoma**

Pathogenesis? Chronic inflammation -> Macrophages produce IL-1 and TNF -> Serum precursor apoSAA in liver -> Degradation by macrophages -> AA amyloid deposition

Associated Conditions? Atrial thrombosis; nephrotic syndrome (proteinuria; hypoproteinemia; hypertriglyceridemia/hypercholesterolemia; edema/hydrothorax/ascites); uremia
Morphological Dx? Causes?

Unilateral or bilateral hydronephrosis and hydroureter
Genetics: C3H, C57L, DDD inbred strains; autosomal recessive mutation in C57BL/6; estrogen implantation in nude mice associated with urine retention; nude mice with Staph intermedius-induced cystitis was reported.


Morphological Dx? Possible case?

Cystolithiasis; unilateral hydronephrosis; unilateral ascending pyelonephritis
Possible case: Proteus mirabilis; Enterococcus spp. and/or Klebsiella oxytoca in NOD-SCID-Il2Rγ (Vet Pathol 48:495-499, 2011) and C3H/HeJ (Toll-like receptor 4 mutation).
Name the Condition?

Mouse Urologic Syndrome

Possible Cause?
Genetics (C57BL/6); Trauma

Name the Condition?

Malocclusion
Possible Cause?
Genetics (C57BL/6); Trauma

6g – 6 weeks old
Developmental delay
Morphological Dx?:

- **Unilateral parotid adenocarcinoma**

Morphological Dx?:

- **Diffuse megaesophagus**
  - Strain association?
  - Aging 129 mice
Viral Diseases of Mice

**Murine Norovirus**
- What viral family? Caliciviridae
- Frequency? Most common virus in lab mice
- Discovered in 2003
- Transmitted by fecal-oral route
- Clinical Signs:
  - NONE in immunocompetent mice.
  - Wasting, diarrhea and death seen in innate immunity deficiencies, especially interferon signaling pathways (first described as lethal in STAT1−/− mice).
- Infects MØ, dendritic and B cells
- Persistence: Months in both immune-competent and deficient mice
- Many field strains: wild mice reservoir
- Infection affected by enteric bacteria

**Possible Causes?**

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**Mouse Hepatitis Virus (MHV)**

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**Murine Norovirus**

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SM Kant, J of Pathology 2015;235,206-216
Possible Causes? Enterotropic mouse hepatitis virus (lethal intestinal virus of infant mice – LIVIM); rotavirus A (epizootic diarrhea of infant mice – EDIM); salmonellosis; Clostridium piliforme; reovirus-3; mouse norovirus

EDIM pups still suckle so observe milk in stomach (top); hydropic vacuolar degeneration of terminally differentiated enterocytes; LIVIM: pups don’t suckle so don’t see milk in stomach

Name of Disease? Mouse Pox or Ectromelia

Ectromelia – D. Percy
**Name of Disease:** Lymphocytic Choriomeningitis Virus  
*Zoonotic*

- **Viral family:** Arenaviridae – related to Lassa virus
- **Most rodents susceptible to infection:** Hamsters are especially sensitive; rats resistant
- **Vertical and horizontal transmission**
- **LCMV can result in asymptomatic clearance and immunity, lifelong persistent infection or rapid death.** CD8+ T cells essential for lethal disease.
- **Viral hepatitis from feeding mouse “pinkies”, death in 24-48 hrs.**

Seizure and paresis following brainstem herniation in immunocompetent mouse. Edema correlates with mortality.  
[Image: LCMV-induced mortality in mice is triggered by edema and brain herniation. CM Matullo, JV, 2010, 312-320]

**Name of virus:** Lactate Dehydrogenase Elevating Virus

- **Family:** Arteriviridae
- **Viral strains are classified as neuropathogenic (C and v) or nonneuropathogenic (P and vx)**
- **Most mice are Asymptomatic**
- **Mouse strains homozygous for Fv1a allele, such as AKR and C57BL/6, will develop poliomyelitis when immunosuppressed. Also reported in ICR-SCID mice.**
- **Age-dependent poliomyelitis requires coinfection with endogenous murine leukemia virus. Murine leukemia virus was present by RT-PCR in all spinal cords.**
- **Poliomyelitis in MuLV-infected ICR-SCID mice after injection of basement membrane matrix contaminated with LDV, Comparative Medicine, 2011, J Carlson**


**Name of Condition? Possible Cause?**

- **Rectal Prolapse**
  - **Possible Cause:** *Citrobacter rodentium*, transmissible murine colonic hyperplasia (MAIDS, Vet Pathol 47:312-317, 2010); *E. coli* (immunodeficient mice); Helicobacter spp. e.g. bilis, typhlonius, mastomyrinus (telomerase deficient mice, Vet Pathol 48:713-725, 2011); enterotropic mouse hepatitis virus (immunodeficient mice); pinworms
What is the name of the upper left condition? **Bilateral papillary thyroid carcinomas**

Morphological Dx?

Morphological Dx? **Pituitary adenoma or adenocarcinoma (hemorrhage)**
2 Morphological Diagnoses? In both cases, Diffuse cystic endometrial hyperplasia, mild to marked. Below left, there is a unilateral ovarian cyst.

3 Different Uterine Conditions. Can you choose which is the muco/hydrometra; which is a graft vs host disease; which is histiocytic sarcoma?

3 Different Uterine Conditions. What might you do to correctly diagnose?
Same Neoplastic Condition, but from different mice. Morphological Dx?

Stomach: Multifocal forestomach squamous papillomas; Vulvar and perineal squamous cell carcinoma

2 Different Conditions; Morphologic Dx? Likely Strain?

Unilateral Testicular Teratoma; Likely Strain? 129
Scrotal Hernia; FVB (Comparative Med 65:391-394, 2012); muscle weakness, estrogen treatment
Dystocia

Likely Cause of Death?

Organ? Common age & strain?

Normal

Seminal Vesicles
Common age & strain? Aged C57BL/6

Dilation (Rt) and Contraction (Lt)
Name of the condition? Likely strain?

Hydrocephalus

Likely strain? Common in C57/BL6


Morphological Dx? Name the Condition? Cause?

Histologic Appearance?

Unilateral Pogranulomatous Mandibular Osteomyelitis, Cellulitis and Dermatitis

Name the Condition? Botryomycosis

Cause? Staphylococcus aureus (Pseudomonas aeruginosa)

Histologic Appearance? Pyogranulomatous to necrosuppurative inflammation, gram positive coci (gram negative rods); Splendore- Hoeppli material
Morphological Dx? Likely Cause?

- Bilateral Tibiotarsal Arthritis

Likely Cause:
- Corynebacterium kutscheri,
- Streptobacillus moniliformis,
- Mycoplasma pulmonis

Parasitic Diseases of Mice

**Nematodes**
- Pinworms (Oxyuriasis)
  - *Syphacia obvelata*
  - *Syphacia muris*
  - *Aspiculuris tetraptera*

**Cestodes**
- *Rodentolepis nana*
  - Dwarf tapeworm
  - Formerly known as Hymenolepis nana
  - Mice, rats, hamsters, humans

**Ectoparasites**
- Mites (acariasis)
  - *Myobia musculi*
  - *Mycopetes musculinus*
  - *Radfordia affinis*

- Lice (pediculosis)
  - *Polyplax serrata*

- Fleas
  - *Leptopsylla segnis*

**Syphacia obvelata**

- Clinical signs
  - Usually asymptomatic
  - Rectal prolapse, intussusception, enteritis, fecal impactions with heavy burdens
Syphacia obvelata
>30% barrier and >70% conventional colonies; Aspicularis tetraptera
Also common
- Pathology
  - No gross lesions, except adults in large intestine
  - Can invade mucosa with inflammation in nudes, and possibly other immunodeficient strains
  - Main research concern is variability in host immune responses
- Diagnosis
  - Tape test (asymmetric eggs Syphacia); Fecal float (symmetric eggs Aspicularis)
  - Highest prevalence 4-5 wk-old mice
  - Examination cecal/colonic contents for adults
  - ELISA: serum antibodies for serum antigens

Cestodes – especially Other
- Taenia taeniaformis
  - Mice, rats, Syrian hamsters, Persian gerbils, occasionally rabbit intermediate hosts
  - Larval form (Cysticercus fasciolaris) usually in liver
  - Focal inflammation, no clinical signs
  - Feed contaminated with cat feces

Mouse Fur Mites – generally mixed infections
- Mycoptes musculinis – most common; severe pruritus BALB/c
- Myobia musculi – severe pruritus-ulcerative lesions with Staph/Strep infections Sensitivity genetically associated [e.g. C57BL/6]
- Radfordia affinis – common, resembles Myobia; no overt disease
- Histopathology
  - Mild epidermal hyperplasia/hyperkeratosis
  - Variable inflammation (L/P, mast cells)
  - Ulcerated lesions; secondary bacteria and fibrovascular proliferation of dermis
  - Mites on surface of lesions, especially early

Questions
1. What is the bacterial agent that affects immunocompromised rodent animal models?
2. Eosinophilic crystaline pneumonia is especially prevalent in which 2 strains of mice?
   - a. BALB/c and C57BL/6 b. 129/SvJ and C57BL/6 c. DBA1 and DBA2 d. FVB and BABL/c
3. Murine norovirus causes what clinical signs in immunocompetent mice?
   - a. Weight loss b. None c. Ruffled fur d. Hunched posture
4. What is the name of the mouse paramyxovirus?
5. A relatively common (and problematic) mouse parasitic infection is?
Spontaneous Mouse Hematopoietic Tumors

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<td>Skin</td>
<td>Rare</td>
<td>Rare</td>
<td>Occasional</td>
<td>Rare</td>
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<tr>
<td>Bone Marrow</td>
<td>Rare</td>
<td>Rare</td>
<td>Occasional</td>
<td>Rare</td>
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</table>

IHC CD3, CD45r(B220), Pax5, CD68, F480

From Table 1 – Ward 2006 Lymphomas and leukemias in mice

What kind of spontaneous neoplasm?
Which organs in this image affected?

B cell Lymphoma
Mesenteric LN & Spleen
Paralyzed Mouse

Causes to consider?
Neoplasia
• Lymphoma
• Histiocytic Sarcoma
• Poorly differentiated osteosarcoma, esp Trp53 mutations
Demyelination
• MHV, TMEV, Induced…
Trauma? Fracture?

Mouse Lung Tumors – Especially A Strain Mice

Adenoma typically, but if large may be Carcinoma
Patterns: Solid, papillary, or mixed
Carcinomas often papillary or mixed and may metastasize to liver

Rats

Rats and associated conditions:
Obesity - Zucker Rat
Diabetes – BB Rat
T-cell deficient – Nude or athymic Rat
Audiogenic seizures – Wistar albino Rat
Hydronephrosis – Gunn Rat (single dominant gene)
Brown Norway and SD - polygenic

Note vibrissae – an athymic rat will have fewer than littermates and they will be coiled/bent

Neoplasia in Rats
**Congenital**

- Hydrocephalus
  - 0.4%-1.4% (noted in HTX, Wistar, various strains)

**Morphological Dx? Possible Cause?**

Chromodacryorrhea

Refers to? Porphyrin pigment

Possible Cause? Rat Sialodacryoadenitis

Coronavirus - Sick Rat!

Stress - How do you distinguish 'blood from the nose and eyes'?

*FIG. 2.12.* - Tubulolobar adenitis (TLA) injection of a rat during the acute stage of the disease. The schematic shows varying degrees of the affected and non-affectued sections, with hematoxylin and eosin stained sections. (Reproduced from *Pathology of Laboratory Animals* by E. A. Hall, copyright 2003 by Wiley & Sons, Inc.)

Ammonia injury to upper respiratory tract
**Name the Condition?**

**Ringtail**

**Cause?** Low humidity; high temperature; hydration; genetics

**Skin**

**Basal cell adenoma/carcinoma**
- Uncommon
- Ribbons/cords/nests of darkly basophilic cells with scant cytoplasm and prominent nuclei

**Keratoacanthoma**
- **Most common adnexal tumor**
  - Crateriform often with keratin horn
  - Arise from hair follicle
  - 3% incidence in aged SD rats, <1% in females
Morphological Dx? **Unilateral, focal, necrohemorrhagic mastitis (left abdominal)**

Cause? *Pasteurella pneumotropica*

---

**Hibernoma**

- Neoplasm arising from brown fat
- High incidence of spontaneous hibernomas in Wistar-Han rats
- Reports of drug-induced hibernomas
- Generally of low incidence (reported cases in humans)
- Commonly seen in thoracic cavity
- Cause labored breathing or posterior paresis if invasive into vertebral column
- IHC for UCP-1 (mammalian thermogenic mitochondrial protein expressed in brown adipocytes).

---

**Morphological Dx?**

**Focal subcutaneous fibroadenoma**

Below is a fixed specimen. Is this cross-section showing the same thing as the image at right? Morphological Dx?

Below is a fixed specimen. Is this cross-section showing the same thing as the image at right? No! Morphological Dx? Below: Unilateral Harderian gland necrosis with interstitial hemorrhage and edema (SDAV); At right: Zymbal's gland adenocarcinoma

Below is a fixed specimen. Is this cross-section showing the same thing as the image at right? Morphological Dx? Below: Zymbal’s Gland Adenocarcinoma

Below is a fixed specimen. Is this cross-section showing the same thing as the image at right? Morphological Dx? Below: Rat Parvoviral Infections

There are 4 serotypes:
- Kilham’s rat virus or RV
- H-1 virus
- Rat Parvovirus – most antigenic
- Rat minute virus (RMV)

- Requires dividing cells, so target tissues?
Rat Parvoviral Infections

- Requires dividing cells, so target tissues?
- Cerebellum, periventricular areas, hepatocytes, endothelial cells, bone marrow

Morphological Dx? Diffuse scrotal dermal hemorrhage
Cause? Kilham’s rat virus

Morphological Dx?
Suppurative bronchopneumonia with bronchiectasis
Cause? Mycoplasma pulmonis

Don’t Forget M. pulmonis; cobblestone appearance and why

FIG. 2.22. Chronic respiratory disease in a rat associated with Mycoplasma pulmonis infection. Note the symmetric involvement of lung lobes and the irregular surface of affected areas due to bronchiectasis and proliferative lymphoid infiltration.

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Don't Forget histopathology of lesion

Arthritis is a rare complication

Morphological Dx? Cause? Name the condition?

Morphological Dx? Likely Cause?

Morphological Dx? Multifocal to Coalescing Necrosuppurative Pneumonia
Cause? Corynebacterium kutscheri
Name the condition? Pseudotuberculosis

Fixed specimen
**Morphological Dx?**  **Interstitial pneumonia**

**Likely Cause?**  Sendai virus (Parainfluenza-1), Pneumocystis carinii – the most common cause of interstitial pneumonia in immunocompetent rats (formerly believed to be rat respiratory virus); rat coronavirus

**Morphological Dx?**  **Multifocal necrotizing myocarditis and hepatitis**

**Cause?**  Clostridium piliforme

**Name the Disease?**  Tyzzer’s Disease

**Morphological Dx?**  **Differential Dx?**
Morphological Dx?  **Multifocal Metastatic Neoplasia**
Differential Dx?  Carcinoma, lymphoma; histiocytic sarcoma; but also could be hepatic abscess due to C. kutscheri, S. pneumonia, K. pneumoniae, P. aeruginosa.

Name the Condition?  **Chronic Progressive Nephropathy**
Histologic appearance?  Thickening of glomerular tufts by eosinophilic material; hyaline casts, dilated tubules with flattened epithelium, interstitial fibrosis, interstitial lymphoplasmacytic aggregates.
Predisposing factor?  Old age, Male, Sprague Dawley strain; high protein diet; immune factors (IgM deposition); hormones (prolactin).
Morphologic Dx? **Unilateral hydronephrosis**
Associated rat strains? **Gunn and Sprague Dawley strains; often right kidney in males due to passage of internal spermatic vessels across ureter**

Morphologic Dx? **Multifocal to coalescing necro-suppurative nephritis**
Cause? **Corynebacterium kutscheri**
Name of the Condition? **Pseudotuberculosis**
Morphological Dx?  
Cystolithiasis, nephrolithiasis and hydronephrosis

Association?  
Lewis/Brown Norway strains with hydronephrosis and renal papillary hyperplasia

• Hematopoietic neoplasia is common in F344, Wistar and Lew/Han
• Most commonly tumors of LN, thymus, spleen and BM
• Generally late onset DZ (> 20 mos) & not as well characterized as in the mouse.
• Lymphoma is rare in the rat (especially compared to mice)
• Leukemia in rats arises in the spleen (vs BM in humans)

Large Granular Leukemia or Mononuclear Cell Leukemia

• Common in F344
• Atypical mononuclear cell leukemia in peripheral blood
• Exhibit NK activity
• Splenectomy reduced incidence.

2 Morphological Dx?

1. Icterus
2. Large granular leukemia of the liver and spleen

Common in F344 and Wistar/Furth rats but rare in other strains. Unknown tumorigenesis mechanism.
Model for human nodular regenerative hyperplasia of the liver?
Name the Condition?

Polyarteritis nodosa
Present in mice (head tilt/vestibular syndrome), primates, dogs (Beagle pain syndrome). Affects medium-sized vessels in any tissue except lung.
Colonic nematodiasis or colonic oxyuriasis

Etiological Dx?

Syphacia obvelata; Aspiculuris tetraperta

Name the Condition? Typical strain?

Peritoneal mesothelioma

Typical strain? F344/N

Blackshear et al., Tox Path 2013
2. Morphologic Dx? Associated rat strain?

1. Testicular interstitial cell tumor – about 90% in F344 rats
2. Mesothelioma of Tunica Vaginalis

Associated rat strain? Both conditions associated with F344/N. Hypercalcemia noted with interstitial cell tumor

Interstitial Cell Tumors
- Also known as Leydig cell tumors
- Uncommon in SD rats
- Almost always benign
- Often bilateral/multiple
- Regulated by LH secreted by pituitary
- Most common testicular neoplasm of the dog, cat and bull; and cryptorchid stallions
- Rare in bird, rabbit, mice and men.

- Yellow-white; multilobular
- Larger tumors may contain hemorrhage, necrosis and mineralization

Morphological Dx? Associated Clin Path?
Morphological Dx?
Focal Pancreatic Insulinoma
Associated Clin Path?
Hypoglycemia

Morphological Dx? Cause?
Bilateral serosuppurative otitis media
Cause? Mycoplasma pulmonis

Morphological Dx? Associated Clin Path finding?
**Morphological Dx?** Chromophobe adenoma of the pituitary pars distalis with compression atrophy of the overlying brain

**Associated Clin Path finding?** Prolactin immunoreactive

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**Rabbits**

**Name the Condition?**
**Cause?**
**Histologic appearance?**

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**Name the Condition?** Fibromatosis
**Cause?** Shope fibroma leporipoxvirus
**Histologic appearance?** Dense subcutaneous fibroblast proliferation with intracytoplasmic inclusion bodies with heterophilic inflammation
Name the condition? Myxomatosis
Cause? Myxomatosis leporipoxvirus

Name the posture? Torticollis
Likely cause? Pasteurella multocida-induced unilateral otitis media; or Encephalitozoon cuniculi, herpes simplex virus J of Comp Path 140:31-37, 2009), or pituitary adenoma

Morphologic Dx? Biologic Dx? Cause?
Morphologic Dx? Proliferative otitis externa
Etiologic Dx? Aural acariasis
Cause? Psoroptes cuniculi

Likely Etiology? Cheyletiella parasitivorax

Likely Biology?

Morphological Dx? Cause? Name the condition? Method to confirm diagnosis?
Morphological Dx? Ulcerative and exudative perineal dermatitis (Ulcerative & Proliferative nasal dermatitis) 
Cause? Treponema paralaiiscuniculi 
Name the condition? Rabbit syphilis, venereal spirochetosis, vent disease 
Method to confirm diagnosis? Warthin-Starry, dark-field microscopy

Morphological Dx? Bilateral ulcerative pododermatitis
Cause? Staphylococcus aureus 
Predisposing factor? Poor sanitation; wire bottom cages 
Name the condition? Sore Hocks
Morphological Dx? Mucopurulent rhinitis
Cause? Pasteurella multocida
Name the condition? Snuffles
D. Percy, Canadian Journal of Comparative Medicine, 1985 49(2):227-230

Morphological Dx? Multifocal aortic atherosclerosis
Pathogenesis? LDL receptor deficient Watanabe rabbit -> hypercholesterolemia & hyperlipidemia -> atherosclerosis
**Morphologic Dx?** Bilateral turbinate atrophy; suppurative tracheitis; Suppurative bronchopneumonia with pulmonary abscessation

**Cause?** *Pasteurella multocida*

---

**Morphologic Dx?** Epistaxis and Multiple pulmonary hemorrhages

**Cause?** Rabbit Hemorrhagic Disease (Calicivirus)

---

**Name the Condition?** Possible Sequela? Predisposing factor?
Name the condition? **Gastric Trichobezoar**

Possible Sequela? **Gastric rupture with peritonitis**

Predisposing factor? **Excessive grooming; decreased gastric motility, sedentary lifestyle**

Morphologic Dx? **Necrohemorrhagic enterointestinalis**

Cause? **Clostridium piliforme**

Name the condition? **Tyzzer's Disease**
Name the Condition? Mucoid Enteropathy

Morphologic Dx? Predisposing factor?

Hepatic lipidosis

Predisposing factor? Obesity, fasting; pregnancy/postpartum; hereditary (deficient LDL receptor Watanabe)

Morphological Dx? Likely Cause?
Morphological Dx? Miliary to coalescing necrotizing hepatitis

Likely Cause? *Clostridium piliforme; Francisella tularensis* (Vet Pathol 47:958-963, 2010); *Listeria monocytogenes; Yersinia pseudotuberculosis; Staphylococcus aureus*

Morphologic Dx? Multifocal biliary cystic ectasia to diffuse proliferative cholangitis with cystic ectasia

Cause? *Eimeria stiedae*
Name? Hepatic coccidiosis
Morphological Dx?
Granulomatous interstitial nephritis with cortical atrophy and fibrosis

Cause? *Encephalitozoon cuniculi*

Shin et al. Seroprevalence of *Encephalitozoon cuniculi* in pet rabbits in Korea, Korean J Parasitol, 2014

Morphologic Dx?
Focal to multicentric uterine adenocarcinoma

Parovarian cysts in the rabbit
Guinea Pigs

Etiologic Dx? Cause?

Guinea Pigs

Etiologic Dx? Multifocal Cutaneous dermatophytosis

Cause? Trichophyton mentagrophytes; Microsporum canis

2 different causes; provide etiologic Dx for image at left; and name the condition for image at right.

Guinea Pigs

2 different causes; provide etiologic Dx for image at left; Cutaneous demodecosis; Cause: Demodex caviae

and name the condition for image at right: Scabies; sarcoptic mange. Cause: Tixacarus caviae
Morphologic Dx? Histologic appearance? Histochemical stain?

**Morphologic Dx?**

**Myocardial Rhabdomyomatosis**

**Histologic appearance?** Vacuolated cardiac myofibers containing granular to eosinophilic cytoplasm (glycogen)

**Histochemical stain?** PAS

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Morphologic Dx? Cause?

**Morphologic Dx?**

**Bilateral suppurative bronchopneumonia**

**Cause?** Bordatella bronchiseptica
**Differential Dx?**

*Suppurative lymphadenitis due to Streptococcus zooepidemicus; thyroid follicular adenoma/carcinoma (Veterinary Pathology 50:334-342, 2012); lymphoma due to caviain leukemia retrovirus*

**Morphologic Dx? Name the condition? Clin Path finding?**

*Hepatic lipidosis*

*Name the condition? Pregnancy toxemia or ketosis*

*Clin Path finding? Hypoglycemia; ketosis; hyperlipidemia*
Morphologic Dx? Etiology?

Necrohemorrhagic typhlocolitis
Etiology? *Clostridium difficile* dysbacteriosis; can be induced by ingestion of topical Neosporin ointment

Name the Condition? Pathogenesis? Other species affected?

**Scurvy**
Pathogenesis? Low dietary vit C -> lack L-gulonolactone oxidase -> low ascorbic acid -> low hydroxylation of procollagen -> inadequate collagen cross linkage -> impaired formation of collagenous support of blood vessels -> periarticular hemorrhages
Other species affected? Primates; fruit-eating bats; some birds and fish, and cetaceans
What is this?

Morphologic Dx? Nasal ulcerative to exudative dermatitis

Pathogenesis? Porphyrin-containing Harderian gland secretions -> nares > no grooming -> irritation > dermatitis +/− Staphylococcus xylosus or S. aureus infection

Gerbils

Morphologic Dx? Cause? Name the disease? Differential Dx?
**Morphologic Dx:** Multifocal necrotizing hepatitis  
**Cause:** Clostridium piliforme  
**Name the disease:** Tyzzer's  
**Differential Dx:** Salmonella typhimurium

**Splenomegaly or splenic hypoplasia in this gerbil?**  
**Possible cause:** Amyloidosis

**Hamsters**

**Biologic Dx:** Cutaneous demodecosis  
**Cause:** Demodex criceti (epidermal pits); D. aurati (hair follicles and sebaceous ducts)
All images due to same cause; Morphologic Dx for image top left? Cause?

Morphologic Dx for image top left? Multifocal cutaneous trichoepitheliomas Cause? Hamster polyoma virus

Multifocal pulmonary ecchymoses and necrotizing hepatitis Cause? Salmonella typhimurium, S. enteritidis
Name the condition? Cause?

Wet Tail

Cause: Clostridium piliforme; C. difficile; Salmonella enteritidis; S. typhimurium; Lawsonia intracellularis

Morphologic Dx? Cause?

Hemorrhagic enterocolitis

Cause: Clostridium difficile
Any Questions?
Thank you!!!